“Cardiac Health Assessment using HRV analysis”

Synopsis of the PhD Thesis

Submitted by

Ulka Shirole

Roll No. 70821015010

Department of Electronics and Telecommunication

Supervisor

Dr. Manjusha Joshi

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V. L. Mehta Road, Vile Parle (West)

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1 Abstract

Cardiac and diabetic diseases are common and troublesome complications, leading to increased morbidity and mortality rates that cause a significant economic burden. In India, the mortality rate is three times higher due to diabetes. Researchers have explored cardiac or diabetic diseases for analysis separately. However, classifying these diseases in a combined group of subjects is necessary for risk assessment before the onset of any symptoms. Diagnosis of cardiac health before pathological conditions becomes critical is crucial. The effect of these diseases on the heart's functionality as time passes, is important for practitioners to suggest medications.

Heart Rate Variability (HRV) is the technique used to study cardiac abnormalities related to fluctuation in sympathetic and parasympathetic activities. HRV is considered a good pointer of autonomic regulator related to cardiovascular health. Researchers have studied HRV in a variety of situations in order to determine the variables that influence it. Autonomous Nervous System (ANS) dynamics are estimated through standard and nonlinear analysis of HRV, which is derived from the electrocardiogram (ECG). HRV offers parameters of autonomous activity which are related to cardiac health.

We performed a retrospective HRV analysis on ECG data of 78 subjects. A decision tree of machine learning is employed to develop an automatic classifier to infer disease implications in the early stages. Furthermore, to cross-verify the above results, an orthostatic stress index is calculated from HRV parameters of ECG data recorded in the sitting and supine positions. Cardiac subjects have the lowest HRV values among the three classes, whereas healthy subjects have the highest. The proposed classification model has achieved an accuracy of 93.58%.

Further, the research contributes to reducing the economic burden of rural people for assessing cardiac health with a degree of correctness equivalent to 2D Echo-cardiography from HRV. We propose a mathematical model that can be used to evaluate 2D echo parameters from HRV data. Next, we studied the deterioration caused due to diabetes in cardiac health. An HRV data in three phases with an interval of six months between two phases is collected from diabetic subjects and analyzed for HRV parameters. Results show gradual deterioration in linear and nonlinear parameters of HRV values from first readings to third, which implies deterioration of cardiac health in people with diabetes. A significant deterioration is observed in OSI and LF/HF parameters.These methods can detect changes before clinical signs appear and can enable early detection and treatment of patients and thus can avoid further complications.

2 Introduction

According to the world health organization (WHO), maximum death is caused by cardiac health issues and contributes to 31% of overall diseases [1]. Cardiac diseases include heart and blood vessel abnormalities leading to myocardial infarction (heart attack). There are various types of cardiac diseases like coronary artery diseases, peripheral artery diseases, cerebrovascular, , etc. The number of subjects suffering from cardiac diseases is rapidly increasing.

Diabetes is another significant disease worldwide that causes dysfunction of various parts of the human body leading to complicated diseases like cardiovascular disease, blindness, neuropathy, cancer, gallstones that sometimes result in mortality [2]. Diabetes cause glucose level to increase in blood that may damage various parts of the body. According to the diabetes atlas 2009, India has 51 million people with diabetes. The mortality rate is three times higher in India due to diabetes, according to a study done by Dr. Mohan, Economics Times Health world, in 2018 [3], where Prognosis of diabetes is almost twice in urban areas compared to rural areas, and urban people spend 33% of their income on diabetes, and rural people spend 27% percent of their income.

Having diabetes and cardiac diseases can affect human health and may lead to heart attack, stroke, and even death. These diseases are caused by various conditions such as poorly controlled high blood pressure, high cholesterol, diabetes, and family history. Due to these factors, the heart supplies insufficiently oxygenated blood as per the needs of the body.

2.1 The Heart Rate Variability(HRV)

Heart Rate Variability (HRV) is a technique used to study heart functionality by analyzing ECG signals. ECG signal is one of the most non-invasive techniques to observe cardiac rhythm. Heart rate variability is the degree of fluctuation in the length of the intervals between heartbeats. They are named *R-R intervals* and are measured in milliseconds (ms). It mirrors the regularity of the heartbeats. Researchers experiment with HRV parameters to find minute changes in ECG signals to assess cardiac health. Greater the regularity, lower the HRV (and vice versa). Figure 1 shows the HRV calculation in the ECG signal. First waveform HRV is more and second one HRV is less as it variation in RR interval is less. HRV is considered a good measure of autonomic control related to cardiovascular health [4, 5]. Cardiac health assessment with the help of HRV analysis becomes popular and beneficial because of its ability to identify minute

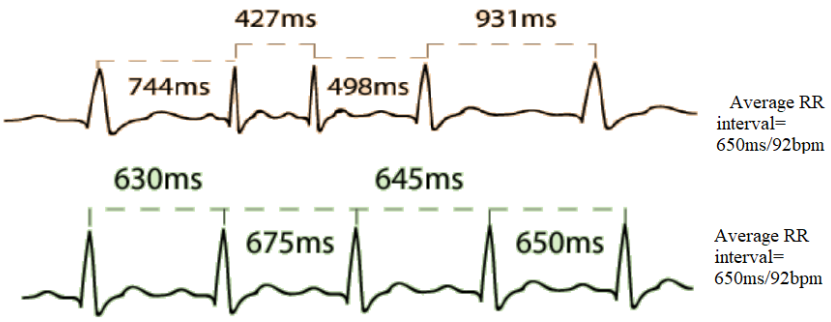

Figure 1: Heart Rate Variability: waveforms showing different R-R intervals

variations in sympathetic and parasympathetic activations [6]. HRV is a direct indicator of the sympathetic and parasympathetic nervous systems. When sympathetic activity predominates, HRV is known to decrease, whereas it increases when parasympathetic activity predominates. HRV thus reflects autonomic control of the cardiovascular system [4].

A balance between the sympathetic and parasympathetic nervous system, called *sympathovagal balance*, is vital for the normal functioning of human heart. The sympathovagal balance is good in healthy subjects. However, its imbalance is evident in subjects suffering from cardiac disease, hypertension, diabetes, or subjects who have undergone heart surgery.

2.2 Motivation

Researchers have applied various techniques for the analysis and prediction of cardiac and diabetic subjects separately. Classification and regression techniques are used by [7, 6] for risk assessment of cardiac patients. Acharya et al. [8] compared diabetic and normal subjects using linear and nonlinear analysis, and it is proved that nonlinear features, sample entropy (SampEn), and approximate entropy (ApEn) show low values for diabetic patients. Fujita et al. [9] predicted sudden cardiac death (SCD) using nonlinear parameters of ECG signal recording that took 5 minutes before SCD onset.

We observe from the literature that, though a separate study on individual categories of subjects is done, a classification of combined diseases is missing. The time from the onset of cardiac and diabetic diseases to its treatment is crucial. Immediate medical facility for such a patient is essential before the patient's condition becomes beyond the physician's control.

ECG provides electrical activity, whereas a more accurate technique 2D echo provides the heart's mechanical functioning but costs ten times more. However, these advanced technological facilities are not easily available in rural areas. In the case of the availability of these

advanced technologies, its cost is so high that it cannot be affordable for common people. There is a need to either upgrade the rural hospitals or suggest a low-cost method to diagnose cardiac health. Our research aims to provide a low-cost method for a cardiac health assessment to warn subjects of their health severity to approach immediate medical treatment. Cardiac diseases and diabetes affect cardiac health causing deterioration in functioning as these diseases remain for a prolonged period of time. To assess cardiac health deterioration with a low-cost method, a three-point HRV analysis is performed to observe the effect of diabetic and cardiac diseases.

Assessment of stress handling capacity is also essential to study the effect of these diseases on the functioning of cardiac health. Therefore, there is a need for some direct index to measure the cardiac health issues, thereby allowing practitioners to judge the subjects' cardiac health.

3 Research Objectives

After a comprehensive literature survey of heart rate variability, we identified the following research gaps:

3.1 Research Gaps

1. Lack of HRV comparative analysis for multi-class cohorts
2. Deficit in stress handling analysis for cardiac health in diabetics, cardiac diseased and normal subjects
3. Lack of periodic HRV analysis in diabetics
4. Need for predicting ejection fraction from HRV parameters to reduce cost of diagnosis

3.2 Research Objectives

This Thesis contributes towards following research objectives based on above research gaps identified in literature

- Statistical analysis of HRV parameters to distinguish cardiac diseased, diabetics and normal subjects.
- Multi-class classification of cardiac diseased, diabetics and normal subjects using machine learning approach

- To rank cardiac health in diabetics, cardiac diseased and normal subjects
- To perform periodic HRV analysis for diabetics using three point study
- To propose a low cost method for predicting ejection fraction from HRV parameters.

4 Literature survey

Researchers have applied various techniques for the analysis and prediction of cardiac and diabetic subjects separately. Classification and regression techniques are used by [7, 6] for risk assessment of cardiac patients. Linear and nonlinear parameters of ECG signals are explored in [10, 11, 8]. The Poincare plot tool is employed to analyze the HRV parameters in [12, 13].

Melillo et al. [6] have proposed a CART-based automatic classifier for the risk assessment of cardiac patients. They have majorly classified patients as low risk and high risk based on long-term HRV parameters. With their proposed approach they have achieved a sensitivity of 93.33% and specificity of 63.3%, however, the sample size used for building the decision tree is small, i.e., 33 patients. The sample size needs to be increased.

Joshi et al. [12] have derived an index from Poincare plot using nonlinear HRV analysis of ECG signal recorded for 3-5 minutes for diagnosis of left ventricular functionality. The proposed index could able to separate the subjects as a control group, hypertensive group, and hypertensive and cardiac group by cross-validating the results using 2D echocardiography. However the index value to rank the subjects from low risk to high risk is required, also diabetic subjects needs to be included.

Acharya et al. [10] analyzed the 2- 5 sec ECG segment morphology for detection of different arrhythmia. ECG is a nonlinear signal, manual analysis might lead to different interpretations from expert to expert. Therefore convolution neural network technique of the computer-aided system diagnostic method is employed to classify the ECG signal as normal, atrial fibrillation, atrial flutter, and ventricular fibrillation with an accuracy of 92.50%. Authors suggested that the robustness and accuracy can further be improved if the database is large and the Keras model is employed instead of k-means cross-validation strategy for validation of CNN technique without filtering for denoising. Cornforth et al. [11] have examined all linear (time and frequency domain) and nonlinear HRV parameters. Various machine learning algorithms are applied to separate subjects from early cardiac autonomic neuropathy from those

of healthy subjects. The genetic algorithm provided the best performance with an accuracy of 70% for maximum separation of two classes, however, declared that the method is not 100% accurate and may vary with classifier algorithm and subset of measures used. Acharya et al. [8] compared diabetic and normal subjects using linear and nonlinear analysis, and it is proved that nonlinear features, sample entropy (SampEn), and approximate entropy (ApEn) show low values for diabetic patients. Using students *t* test to all nonlinear parameters like standard deviation (SD2), Recurrence plot (REC), Detrended Entropy (DET), ApEn, SampEn, and correlation dimension (CD) to distinguish the normal and diabetic subjects.

Fujita et al. [9] predicted sudden cardiac death (SCD) using nonlinear parameters of ECG signal recording taken 5 minutes before SCD onset. The paper classifies normal subject and SCD subjects using K- nearest mean (KNN), Decision Tree (DT), and support vector machine (SVM) algorithms of machine learning. Nonlinear features which are ranked using *t* value of Renny entropy, Fuzzy entropy, Hjorth's parameters, energy features of discrete wavelet transform and Tsallis entropy. Among all classifiers, SVM gave the best results that predicted SCD four minutes before its onset with an accuracy of 94.7% thus providing clinician a warning sign for urgent treatment. Table 1 provides literature survey in chronological order. The table 1 provides extensive literature survey in chronological order. The objectives set for the proposed research will contribute to fill gaps.

Table 1: Literature Survey

Sr.no	Author, Year, Publisher	Sample size	Methodology	Conclusion
1.	Muscholl et al. (2002) [14] International Journal of Cardiology	132 MI and chest pain	Echo and ECG ST elevation	seperated severe MI from mild MI using combination of ECG ST and Echo
2.	Kim et al. (2005) [15] American Roentgen Ray Society, ARRS publisher	19 subjects	LVEF using ECG gated MDCT	Ejection fraction measured by cardiac MDCT yielded a significant overestimation of 2.9% ± 8.7% (mean ± SD) compared with that measured by echocardiography.
3.	Seyd et al. (2008) [16] International Journal of Biological and Life Sciences	16 DM and 16 Control group	HRV	significant diffrence between HRV time and frequency domain parameters in DT and control group

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Table 1 –*Continued from previous page*

Sr.no	Author, Year, Publisher	Sample size	Methodology	Conclusion
4.	Pecchia et al. (2011) [7], IEEE Transactions on Biomedical Engineering	83 Normal 54 HF(12 mild and 17 severe)	CART	Remote health monitoring using CART for Heart Failuer (accuracy$\bar{9}$6.39%)
5.	Faust et al. (2012) [17] Biomedical Signal Processing and Control, Elsevier publication	30 (15 Dia and 15 Normal)	HRV	Nonlinear parameters are supirior to linear
6.	Melillo et al. (2013) [6] IEEE Journal of Biomedical and Health Informatics , 2013	30 Low risk and 11 High risk subjects	CART	seperates low risk patients from high risk one using HRV
7.	Joshi et al. (2013) [12] International Journal of Scientific & Technology Research	30 control and 22 HT subject	HRV	proposed a confirmative tool for diagnosis using pioncare plot
8.	Risum et al. (2013) [18] American Heart Journal, Elsevier publication	66 LBBB subjects	Concordance in ECG lead voltages and LVEF	a close relation between electrical activation by ECG and mechanical contraction by echocardiography demonstrated, that will help to identify CRT candidates.
9.	RajendraAcharyaetal.(2015) [19] Knowledge-based systems, Elsevier publisher	15 DM 15 Healthy	HRV, ML	Classified DM from Control subjects and showed SVM is the best
10.	Joshi et al. (2015) [20] Bitish Journal	27 Normal, 39 D and 40 HT	Corr and HRV	Goodness of fit test insignificant therefore SDNN cannot predict LVEF
11.	Fujita et al. (2016) [9] Applied Soft Computing, Elsevier publisher	20 SCD and 18 Normal	HRV , ML	97.3%, for prediction of SCD one minutes prior to onset using SVM
12.	Cornforth and Jelinek (2016) [21] Computing in Cardiology Conference (CinC),	18 Normal and 15 CHF	DT and NN	Renyi entropy in addition to standard time domain measures identified CHF with higher accuracy (87.9%
13.	Kumar et al. (2016) [22] Expert Systems with Applications, Elsevier Publication	10 healthy and 10 CAD subjects	HRV Fuzzy entropy,KNN	100% accuracy using LS-SVM Morlet and Radial Basis Function (RBF) kernels for dignosis of CAD
14.	Acharya et al. (2017) [10] Information Sciences, Elsevier publication	148 MI 52	healthy & Deep CNN	identified normal and MI subjects (accuracy-93.53%)

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Table 1 –*Continued from previous page*

Sr.no	Author, Year, Publisher	Sample size	Methodology	Conclusion
15.	Leren et al. (2017) [23] Cardiovascular Imaging, Elsevier	86 index patients and 76 mutation-positive	Genetic and statistical analysis	S ECG parameters, RV diameter, and RVMD were markers of previous arrhythmic events in patients with early ARVC

5 Brief Summary of Contributions

5.1 Distinguished between diabetics and cardiac diseased subjects using statistical analysis- A Preliminary Work

Cardiac health issues are severe and cause maximum death according to the survey done by the world health organization. The time from the onset of cardiac diseases to the treatment for the same is very crucial. Immediate medical facility for such patients is essential before the patient's condition becomes beyond the control of the physician. The onset of cardiac diseases results in changes in the ECG signal of patients. These changes can be used as a tool for diagnosis. In such cases, if the disease is confirmed severe the paramedical staff can start the preparatory treatment before the physician arrives.

Data Collection: Clinical data is collected from 91 subjects, from cardiac diseased, diabetic diseased and normal or healthy subjects from B & J Superspeciality hospital, Navi Mumbai, using 12 electrode ECG aquisition machine Subjects involved in the study have ages in the range of 30–65 years.

Methodology: HRV is diagnostic tool that shows minute variation that reflects autonomous nervous system dysfunction due to diseases. Here we have used descriptive statistical tools such as mean and standard deviations for each class of subjects. To check whether these group of subjects can be distinguished from one another, we tested for p value ($p<0.05$).Following HRV parameters were analysed.

1. **Time Domain Analysis:** Time domain analysis includes the measurement of parameters like RR interval, standard deviation of NN interval (SDNN), standdard deviation of the average NN interval (SDANN), heart rate (HR), percentage of number of successive NN interval which differ by more than 50 ms (pNN50) and root mean square root of successive difference (rMSSD). These parameters are calculated from variation in the intervals between successive cardiac cycles.
2. **Frequency Domain Analysis:** Frequency domain analysis describes in principle the oscillations of the heart rate signal, decomposed at different frequencies and amplitudes, and provides information on the amount of their relative intensity in the sinus rhythm of the heart. The frequency domain is based on different frequency areas in the time series. The power spectral density is measured by calculating FFT (fast Fourier transform) of the time series. Typical variables include VLF (very low-frequency power), LF (low-frequency power), HF (high-frequency power), total power, and LF/HF ratio (sympatho-vagal balance).
3. **Nonlinear parameters Analysis:** It is based on the fact that the ECG signal is non-stationary. The non-linear method can start without specifying any fixed pattern in the signal, but simply looking at similarities in the signal. In the non-linear analysis, Poincare plot and entropy are used [24].

Results

Table 2: Overall Significant parameters in Statistical analysis

Features	Normal (mean±SD)	Diabetic (mean±SD)	Cardiac (mean±SD)	p value
SDNN	77.27±97	64.13±54	41.28±31	<0.01
SD2	84.57±87	71.25±44	47.24±24	<0.03
NN50	103.4±176	98±213	64.2 ±110	< 0.05
HF	8581.7±5619	3227±2099.2	1088.39±233	<0.05
LF/HF	2.20± 1.66	2.077± 2	1.66± 1.47	<0.05
SD1	65.36±109	51.4±66	30.5± 39	<0.05
ApEn	1.21± 0.43	1.16± 0.30	1.01± 0.41	<0.05

Table 3: Comparison of current work with contemporary work

Para meters	**Literature 1**		**Literature 2**		**Literature 3**		**Proposed method**		
	Acharya et al. [8]		**P. T. Ahamed Seyd** [25]		**Paolo Melillo** [6]				
	Normal	Diabetic	Normal	Diabetic	Lower risk	Higher risk	Normal	Diabetic	Cardiac
Data	**15**	**15**	**16**	**16**	41 CHF		26	30	35
Method	HRV		HRV		CART		DT		
HR	69	84	66	84			77	81	84
SDNN			46.4±99.2	15.3 ± 14.7	399	90	77.27	64.13	41.28
NN50	118	31	582.8	83.2			103.4	98.75	64.22
pNN50	14.4	3.46	19.4	2.76	3.02	1.7	10.45	10.5	8.09
VLF			371.8±354.8495	49.2±85.3148	12553	622	1299	8460.2	575.5
LF			476.4±307.2401	55±123.1025	28813	595	2856	1874	646
HF	272	87	260.7±237.2959	85.7±223.3766	60783	1691	8581	3227	1088
Total Power					132516	6718	49527	6425	2316
LF/HF	2.49	2.05	2.5722±1.3967	1.4812±1.4019	0.45	0.46	2.077	2.2	1.66
SD1							65.36	51.4	30.5
SD2	64.9	30.9					84.57	71.25	47.24
ApEn	1.33	1.18					1.21	1.16	1.01
Parameters	all HRV		linear		SDNN,Tot.Power,pNN50		ApEn,SampleEn,Lf/Hf,pNN50		

Table 2 shows the results of statistical analysis of HRV parameters. All HRV parameters were analysed for statistical mean amd standard deviation and were tested for p value. It is evident that, parameters namely SDNN, SD2, NN50, HF,LF/HF,SD1 and ApEn are significant parameters for class separation as the p value is less than 0.05. Since sample size is small, students *t-test* is used to calculate p value [26, 19, 6, 9]. Also the mean value of three class of subjects shows significant difference for the said parameters. From Table 2 we see that values are lowest for cardiac diseased subjects leading to increased risk. The HRV values are highest for normal class of subjects being at lowest risk and diabetes subjects are at moderate risk with the HRV value lying between cardiac diseased and healthy ones.

Discussion

HRV is a widely adopted quantitative marker of the autonomic nervous system which can be used as a predictor of risk for humans to develop cardiovascular diseases. Moreover, decreased heart rate variability (HRV) has been associated with an increased risk of cardiovascular diseases. The standard deviations of NN (RR) intervals, SDNN, is a global index of HRV. It is normally calculated using the standard deviation of normal QRS distances.

Reduced SDNN value means reduced duration between two heart rhythms, that implies increased heart rate. It is true since in cardiac diseased subjects due to presences of blockages in arteries (subjects for this experiment), implies increased pressure on heart to pump blood to meet body's blood demand. In case of diabetes subjects increased sugar level causes dysfunction in myocardium, and hence the heart exerts more pressure to meet body's blood requirement, hence heart rate increases and SDNN is observed reduced. P value <0.05 for NN50 and SDNN signifies that these HRV parameters are most significant and they distinguish cardiac diseased (higher risk) for diabetics (lower risk) as shown in Table 2.

The NN50 value provides number of consecutive RR intervals which differ by more than 50 ms. Heart rhythms should not be of constant duration. Heart is a nonlinear system. Many factors affect it including respiratory system. NN50 count distinguish normal subjects from cardiac diseased [27]. The consecutive RR intervals with duration 750 ms and 800 ms implies 80 bpm and 75 bpm heart rate. Difference in RR interval less more than 50 ms indicates good variation in HRV, to account for influence due to other factors. The reduced value of NN50 indicates parasympathetic deactivation. Atherosclerosis cause resistance to blood flow in blood vessels. A particular portion of the heart will not receive proper blood supply and cause myocardial damage, which causes parasympathetic deactivation. The presence of elevated glucose particles cause deoxygenated blood supply to cardiac muscles, causing cardiomyopathy, resulting in elevated heart rate and parasympathetic dysfunction, which result in reduced HRV. The p value calculated using students t test provides statistical significance. The mean value of HRV parameters ranks the subjects from higher risk to lower one.

In frequency domain term LF/HF reassembles sympatho-vagal balance. In the frequency domain, the ratio of low frequency to the high frequency is used to detect cardiomyopathy abnormalities. In the PSD, two major oscillatory components are usually detectable:One synchronous with respiration is described as high frequency (HF) (about 0.25 Hz and varying with respiration [31]), whereas the other, corresponding to the slow waves of arterial pressure, is described as low frequency (LF) (about 0.1 Hz). The LF/HF ratio is considered an index of cardiac sympathetic/parasympathetic tone balance [32]. HRV in patients suffering from diabetes or cardiovascular

diseases reveal a reduction in total and in the individual power of spectral components. The presence of an alteration in neural control is also reflected in a blunting of day-night variations of RR interval. The p value for HF and LF/HF and HF is <0.05, implies separation of diabetics and cardiac diseased subjects using these parameters is valid.

In Table 2, SD1 and SD2 from poincare plot indicates short term and long term variability, with SD2 greater than SD1. The Poincare plot, a technique taken from nonlinear dynamics, can be used to portray the nature of RR interval fluctuations [28]. In the plot, each RR interval is plotted as a function of the previous RR interval. The plot for the normal subject is ellipse-shaped and aligned at the center with SD2 longer than SD1, which means more long term variability than short range variability. The same is true for the diseased subject, but both SD1 and SD2 are lower. These differences explain the low p-values reported in Table 2 Acharya et al. [8] has classified subjects as normal and diabetics, using all HRV parameters.P. T. Ahamed Seyd [25] separate normal subjects from diabetics using only linear parameters. The parameters shown in table are significant($p<0.05$) to separate diabetics from cardiac diseased. These values are lowest for cardiac diseased, moderate for diabetics and highest for healthy subject. The results show that the selected features are all clinically statistically significant. Therefore, we conclude that the findings here can be used as a tool for diagnostic purposes.

5.2 Devised formula for OSI index that ranks subjects from high risk to low risk

Diabetes is a chronic disease characterized by hyperglycaemia, which leads to specific long-term complications: retinopathy, neuropathy, nephropathy and cardiomyopathy. Congestive heart failure (CHF) is a pathophysiological condition due to an abnormal cardiac function, which is responsible for the failure of the heart to pump blood as required by the body.Analysis of cardiac health using heart rate variation (HRV) has become a popular method to assess the activities of the autonomic nervous system (ANS). It is beneficial in the assessment of cardiac abnormalities, because of its ability to capture fast fluctuations that may be an indication of sympathetic and vagal activity.

The assessment for cardiac health requires to analyze sympathetic and parasympathetic systems. Here in this experiment ANS is analysed from ECG data collected in supine and sitting position. An index called orthostatic stress index is devised that ranks the subject from high risk to low risk.

Data Collection:

In this study, clinical data is collected for a total of 60 subjects, from diabetics, cardiac diseased and normal or healthy subjects. Subjects involved in the study are having ages in the range of 30-65 years. ECG data were collected for these patients, from B and J super specialty hospital Kamothe, Navi Mumbai. Patients' ECG data is collected using a 12 electrode ECG acquisition machine based on the PC ECG software. The PCECG software acquires data of all 12 channels and stores it in an XML file. ECG data is recorded for 15 minutes in a sitting position and 15 minutes in a supine position.

Methodology:

Kubios, an HRV analysis software, provides time domain and frequency domain information. Kubios analysis information is used for cardiac health assessment. It provides time domain parameters such as mean RR interval, SDNN, mean RR, NN50, and pNN50, and frequency domain parameters such as power in the VLF (0-0.04 Hz), LF (0.04-0.15 Hz), HF (0.15-0.4 Hz) and LF/HF ratio. Figure 3 shows the R-R interval distribution histogram and

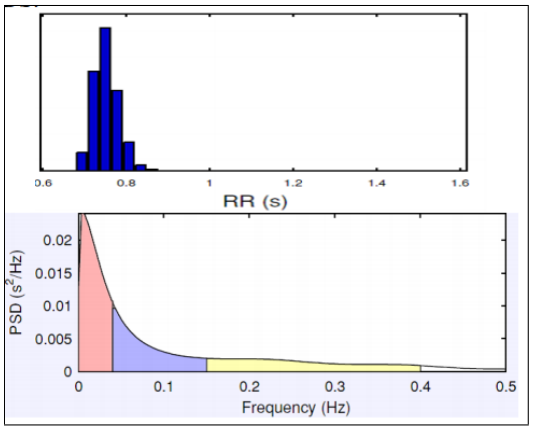

Figure 2: Histogram and PSD of cardiac subject

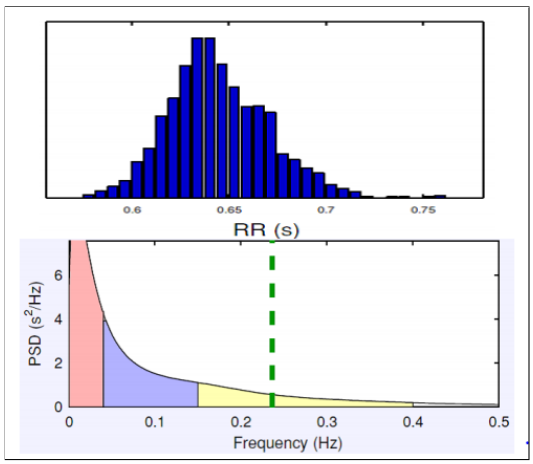

Figure 3: Histogram and PSD of normal subject

the AR spectrum of a healthy subject in a supine position. Figure 2 shows the R-R interval distribution histogram and the AR spectrum of a subject with cardiac disease in a supine position. From figure 2 and figure 3, it is evident that the R-R interval spread is more for healthy subjects compared to the cardiac disease subjects. Moreover, the AR spectrum of both subjects looks similar, but their power spectral density (PSD) is different. In other words, healthy subjects have high PSD and diseased subjects have low PDS. In the frequency domain, the ratio of low frequency to the high frequency is used to detect cardiomyopathy abnormalities. In the PSD, two major oscillatory components are usually detectable: One synchronous with respiration is described as high frequency (HF) (about 0.25 Hz) and varying with respiration [29], whereas the other, corresponding to the slow waves of arterial pressure, is described as low frequency (LF) (about 0.1 Hz). The LF/HF ratio is considered an index of cardiac sympathetic/parasympathetic tone balance [30]. Human body position considerably stimulus cardiac autonomic drive. Autonomic balance is clearly different when subject's body position is changed i.e.between supine and sitting positions. Parasympathetic nervous function predominates in supine positions, while sympathetic function predominates in sitting positions. The effect of these positions on healthy subjects and disease subject gives significant information on the cardiac health of subjects. Based on the information collected, we define an empirical formula called *"Orthostatic Stress Index"*, which gives a rank to the subjects based on their cardiovascular health. This index is based on the sympathovagal balance of supine and sitting positions. It is expressed as

$$OSI = \frac{(LF/HF)_{sitting} - (LF/HF)_{supine}}{(LF/HF)_{sitting}} \tag{1}$$

where, LF/HF is a ratio of sympathetic power to parasympathetic power. This ratio is expected to be low in the supine position because parasympathetic power dominates sympathetic power in the supine position.

PID	Cardiac	Diabetes	$(LF/HF)_{supine}$	$(LF/HF)_{siting}$	OSI
1	YES	YES	8.739	2.014	-3.33913
2	YES	NO	6.297	1.601	-2.93317
3	YES	NO	1.8509	0.47871	-2.86643
4	YES	YES	0.299	0.084	-2.55952
5	YES	YES	5.5319	2.0686	-1.67422
6	YES	YES	2.6439	1.1289	-1.34201
7	YES	NO	1.0249	0.55206	-0.8565
8	YES	NO	4.303	2.346	-0.8341
9	YES	NO	0.58602	0.41572	-0.40965
10	YES	YES	0.92879	0.73383	-0.26567
11	NO	YES	5.5809	4.4766	-0.24668
12	NO	YES	1.253	1.1056	-0.13332
13	YES	YES	0.568	0.524	-0.08397
14	NO	YES	0.70649	0.67859	-0.04111
15	NO	YES	0.70649	0.70649	0
16	NO	YES	0.1902	0.1902	0
17	NO	YES	3.7997	3.7997	0
18	NO	YES	1.3189	1.3189	0
19	NO	NO	8.162	8.2367	0.009069
20	NO	YES	1.533	1.884	0.186306
21	NO	NO	1.9908	2.5121	0.207516
22	NO	NO	4.031	5.185	0.222565
23	NO	YES	3.647	5.017	0.273072
24	NO	NO	3.7997	5.4918	0.308114
25	NO	NO	2.0686	3.1875	0.351027
26	NO	NO	0.19837	0.32275	0.385376

Figure 4: OSI ranks the subjects from high risk to low risk

Table 4: Comparison of proposed work with contemporary research

Research	Data	Method	output	conclusion
Petrofsky et al. [31]	35	OS-tilt	cardiac output, Heart Rate	for diabetics parameters reduced
Schneider et al. [32]	12	tilt testbefore and after 48hr rest	heart rate and systolic BP	decline in diabetics
Joshi et al. [12]	60	OSI index	mean value of OSI	more for normal ,decline for diabetics
Proposed System	**60**	**OSI index**	**actual OSI values**	**OSI ranked cardiac health from high risk to low**

Results:

Table 4 summarizes LF/HF ratio and OSI for 26 subjects and their clinical symptoms. The subjects are from different category. Subjects with cardiac diseased, diabetes and hypertension, have one or other factor as mentioned. Supine data indicates parasympathetic dominance and data in sitting position indicates sympathetic dominance. Hence the OSI calculated provides information regarding stress handling capacity of heart. Comparing OSI values with clinical symptoms, it is notices that subjects having cardiac diseases have low stress handling capacity. The healthy subjects have positive OSI. Greater value of OSI implies an healthy heart implying better stress handling capacity. The subjects are ranked in the table according to OSI value, and it is observed that there is a correlation between OSI index and clinical symptoms.

Discussion:

The OSI ranks the subject from high risk to low risk. OSI is dericed from sympathovagal balance(LF/HF). As LF is related to sympathetic power and HF with parasympathetic power, HF power is low in the supine position (parasympathetic power) and LF is high in the sitting position (sympathetic power). In subjects suffering from cardiac diseases and diabetics, sympathovagal balance is not maintained because of reduced performance of the heart. From the calculations, it is observed that OSI index is low for cardiac patients as is expected.

Table 4 shows the contemporary work. Researchers have performed stress test in different ways. petrofsky et al exerted stress by making subject to stand. cardiac output and heart rate were measured before tilt and after tilt for normal and diabetic subjects, Reduced parameter value is observed for diabetics. schneider et al performed tilt test for normal and diabetics before and after 48 hours of rest and measured heart rate and systolic blood pressure. For diabetic patients the parameters were declined. Joshi et al calculated mean OSI value for diabetics and normal subjects and observed lower mean OSI value for diabetics. Our index value ranks the subjects from high risk to low risk.

5.3 Decision tree model for classification of cardiac diseased, diabetics and normal subjects with 93.58% accuracy

The heart is a complex control system that is affected by various factors like sedentary lifestyle, physical, mental stress, chronic diseases, etc. [33]. Diabetes and cardiac disease can affect human health and may lead to heart attack, stroke, and even death. As it is proved in our earlier experiment that cardiac diseased subjects are at highest risk. Researchers have explored classification of cardiac and normal subjects and diabetics and normal subjects. It is necessary to know deterioration in cardiac health due these cardiac diseases and diabetes or improvement due to surgery or medication. For this it required to perform multi-class classification of the subjects. In our experiment we have analyzed HRV signals of diabetics, cardiac patients, and normal subjects using linear and nonlinear parameters of HRV in the supine position to classify diabetic, cardiac, and normal patients. The proposed classification model has achieved an accuracy of 93.58%, precision, and recall of 94% by combining linear(time domain and frequency domain) and nonlinear HRV features.

Data collection:

ECG recording of 97 subjects of diabetic, cardiac diseased and normal were collected in sitting and supine positions, at B & J Superspeciality Hospital, Navi Mumbai, India. After removing outliers 78 subjects were remain for analysis.

Methodology:

Workflow of proposed system: The detailed workflow of the process is shown in figure. 5 having four stages. In the first stage, data is collected using 12 electrodes ECG. In the second stage, the data of the second

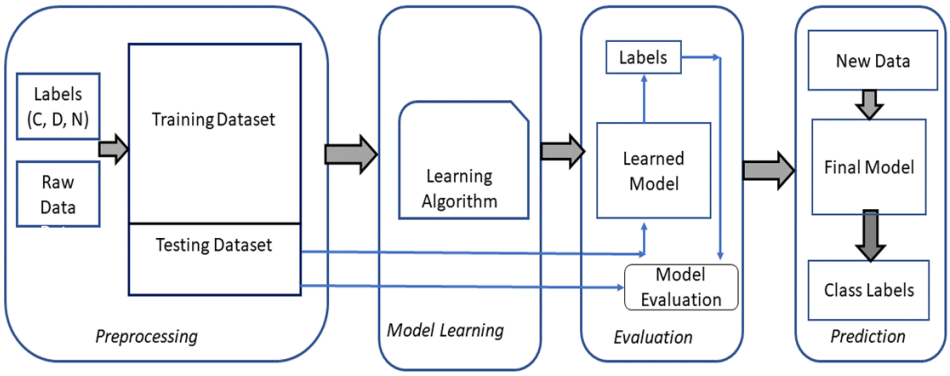

Figure 5: The workflow of the process for data capturing, analysis and classification.

channel is used for further analysis. In the third stage, HRV analysis is carried out using Kubios software (available at: http://kubios.uku.fi). The various linear and non-linear HRV parameters are used in the classification stage. Initially, Labels are assigned to subjects as: D - diabetic, C - cardiac, and N - normal according to the physician's

diagnostic report. In the fourth stage, the supervised machine learning method is employed to train a model. Details of the machine learning process are discussed in the next section.

Machine Learning Technique: Machine learning algorithms are used to train machines to take decisions/ predictions based on data input. In this work, we are considering a supervised algorithm. There are four main processes: 1) pre-processing, 2) model learning, 3) model evaluation, and 4) class prediction of new data. For the sake of simplicity, we discuss the decision tree algorithm which we have used in our work.

The algorithm for building a decision tree employs a top-down greedy search starting from the root node that corresponds to the best predictor for possible branches to a leaf node. Commonly used criteria for splitting is *Gini index*, whose value ranges from 0 to 1. The Gini index zero indicates that all records at the node belong to the same class, and Gini index one indicates that all records belong to different classes.

Gini index for classification at each node t in a tree can be defined as follows:

$$Gini\ index = 1 - (n_c/N)^2 - (n_d/N)^2 - (n_k/N)^2$$

where, N is the total number of subjects; n_c - # cardiac subjects, n_d - # diabetic subjects and n_k - # normal subjects.

Results

We carried out the experiment in two stages. In the first stage, we carried out experiments of time domain, frequency domain, and non-linear parameters separately. In this stage the classification accuracy obtained is 86.60%, 80.41%, and 84.54% respectively. In the second stage, based on the results obtained in the first stage experiments, we selected a group of attributes from each domain for the final classification. The algorithm was tested for different models with heights ranging from 2 to 10. The set of attributes selected for final model generation are pNN50, LF/HF, SampleEn and ApEn. We have tried Figure 6 shows the depth 7 classification tree. It was observed that after certain tree height, accuracy drops or remains constant and does not improve. A reduced height tree is easy to understand and apply but is more general and does not give the required accuracy. A complete height tree is complex and gives the highest accuracy but not a good model for test data. In other words, as we reduce the tree height tree gets pruned to generalize the model at the same time we lose accuracy. So there is trade-off between accuracy and tree selection.

The classification summary of the model is as shown in Table 5. The average precision, recall, and F1- score of the model is 94%. This indicates that the exactness and completeness of the model is good i.e.94%.

Discussion

We have developed decision tree algorithm which will classify cardiac deseased , diabetics, and normal subjectsclassification with an accuracy of 93.58%. The result shows that there is some miss-classification in cardiac and diabetic subjects. Therefore, we decided to cross-verify the reason for the miss-classification using the OSI index as the risk factor of the subjects. The OSI index of the sample subjects is shown in Table **??**, which shows the PID (patient ID), labeled class, predicted class, and orthostatic stress index for diseased and control subjects. The table also shows subject's details regarding medical history, symptoms noted from the patient's file as diagnosed

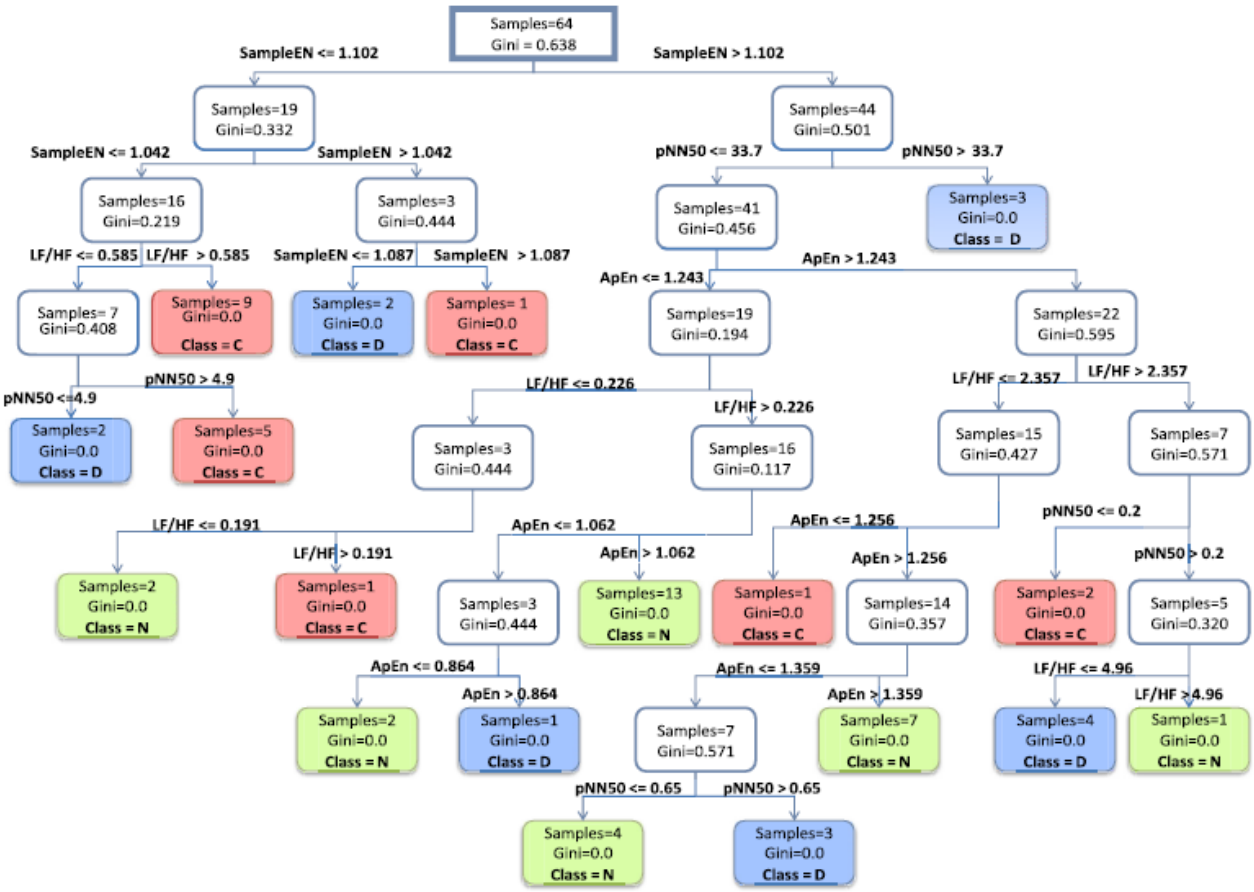

Figure 6: Decision tree for using combined features:

Table 5: summary of classification report.

Subjects	Precision	Recall	F1-score
Cardiac	0.96	0.92	0.94
Diabetic	1.00	0.82	0.90
Normal	0.90	1.00	0.95
Average/Total	0.94	0.94	0.94

Table 6: Comparison of proposed work with contemporary research

Research	Data	Method	Accuracy	Parameters
Giannakakis et al. [34]	24	CART	84.50 %	pNN50, LF/HF, HF, RMSSD
Comforth et al. [21]	33	NN	87.90 %	RennyEn, SDNN, RMSSD
Paolo Melillo [6]	44	CART	85.40%	SDNN, Tot.Power, pNN50
Proposed System	**78**	**Decision Tree**	**93.50%**	**ApEn, SampleEn, LF/HF, PNN50**

by the cardiologist. Some miss-classifications in classification are due to the model. However we have also noted that some miss-classifications are due to change in the state of subjects due to medical operation or continuous medication. For example, PID P25 was initially labeled as cardiac, but predicated by the decision-tree model as the normal subject because, he went through medical surgery where his 4 blockages were removed, and 2 stents were placed. Similarly, PID P40 was initially labeled as a diabetic but predicted by the decision-tree model as the normal subject because subject is taking regular medication. OSI index has given correct reasoning for the prediction.

Table 6 shows comparison with contemporary work. Giannakakis et al classified normal subjects and diabetics using CART algorithm of machine learning with 24 dataset and achieved an accuracy of RennyEn, SDNN, and RMSSD. Cornforth et al applied NN algorithm of on 33 dataset of cardiac diseased and normal subjects with an accuracy of 87.90%. our proposed system has achived an accuracy of 93.50%. This proposed model can be used to predict and give concerned warning to the clinicians regarding cardiac or diabetic symptoms of patients. OSI has confirmed the accuracy of the classification model and reasoning for the mis-classification of some subjects.

5.4 LF/HF and OSI are most significant parameters that provide minute variations due to diabetes over the period in all patients

Diabetes cause heart dysfunction. Early detection of sub-clinical autonomic dysfunction in diabetic individuals is important for risk stratification and subsequent management, possibly including pharmacologic and lifestyle interventions [35]. It is necessary to perform periodic analysis to observe the deterioration rate due to these diseases. A three phase HRV analysis is performed to study deterioration in cardiac health due to diabetes. The data collected here is for 15 minutes is useful than short time ECG recording, that it provide a more complete description of HRV dynamics, because during this long recording period, the subject will experience many different stimuli, and the autonomic nervous system is probed in a variety of situations.

Data Collection:

ECG recording for 31 subjects, suffering from diabetes is collected using 12 electrodes ECG acquisition machine, for 15 minutes in supine and sitting positions. The data of same subjects is collected in three phases with a 6 months duration between two records.

Methodology:

Statistical tool, mean of hrv parameters were calculated for analysis.

Result:

Figure 7 shows that there is gradual decline in hrv parameters. Significant parameters are SDNN, LF/HF,OSI, and SampleEn. This indicates that diabetes gradually deteriorates the cardiac health. Figure 8 and figure 9 shows change in hrv values from phase-I reading to Phase-III reading. It is observed that LF/HF and OSI reflects minute variation due to diabetes than other hrv parameters such as SDNN, HR and sampleEn. This is because diabetes cause sympathetic and parameters nervous system deteriorate. In figure 7 shows percentage deterioration from phase-I to phase-II and from Phase-II to Phase-III. LF/HF and OSI deterioration is more than other parameters.

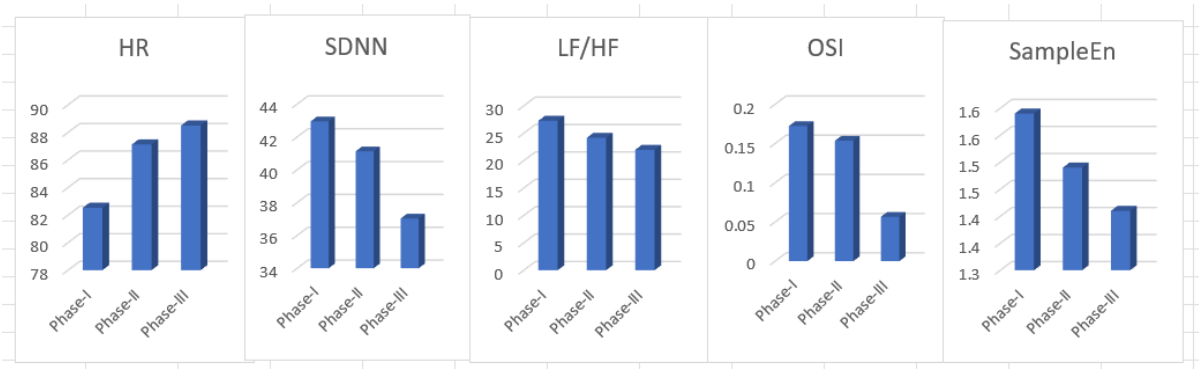

Figure 7: Three phase deterioration study

Discussion:

As compared to LF/HF and OSI parameters SDNN, and sampleEn, and HR are less sensitive parameters as reflected in graph. OSI is more sensitive parameter. Reduced value of LF/HF indicates parasympathetic dominance, but OSI accounts for both PNS and SNS activation. Lower value of OSI indicates reduced SNS activity due to diabetes. [36](range of hrv values). Also SDNN and HR accounts for RR interval duration and not for the signal strength. Since diabetes affects sympathetic and parasympathetic nervous system which is directly reflected in LF/HF and OSI. These methods can detect changes before clinical signs appear. So we can expect that these measures enable early detection and treatment/subsequent management of patients and thus can avoid acute and chronic complications.

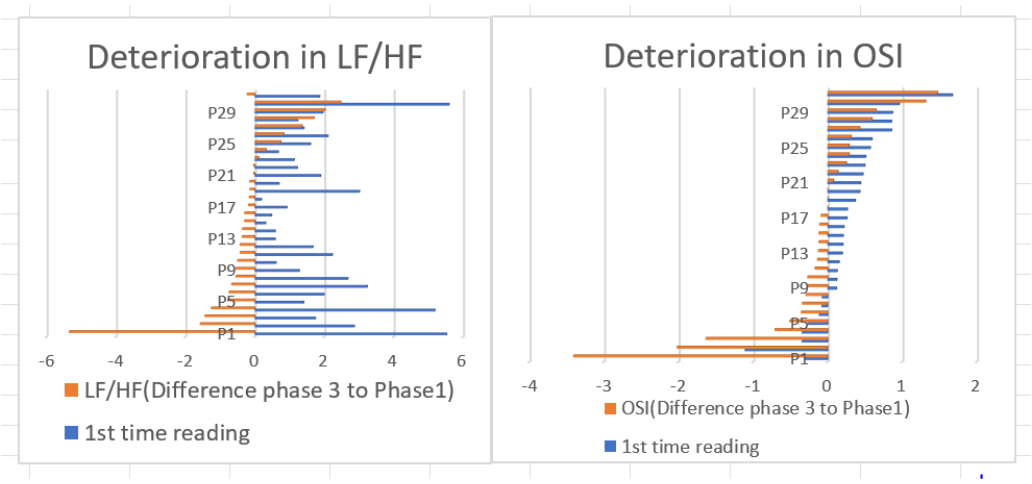

Figure 8: Deterioration in LF/HF and OSI from phase-I to phase-III

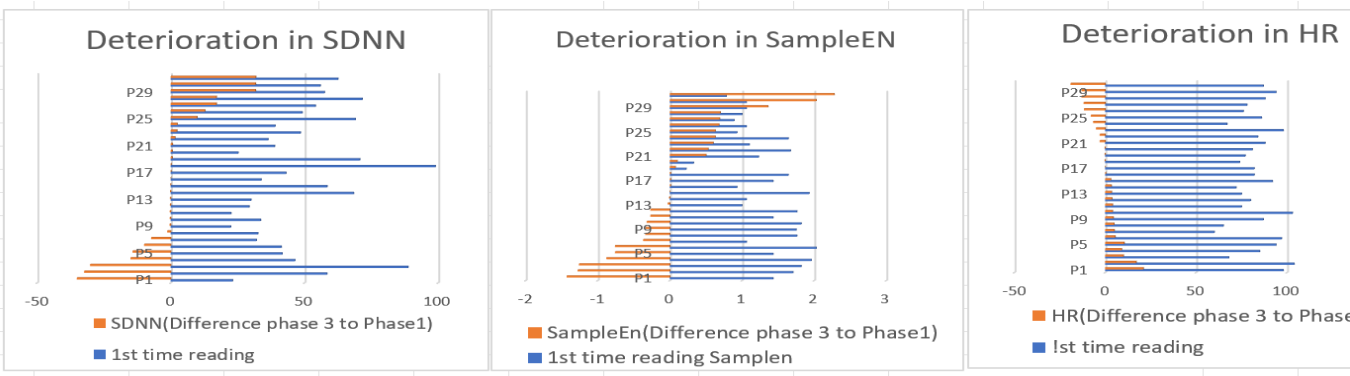

Figure 9: Deterioration in SDNN, SampleEn and HR from Phase-I to Phase-III

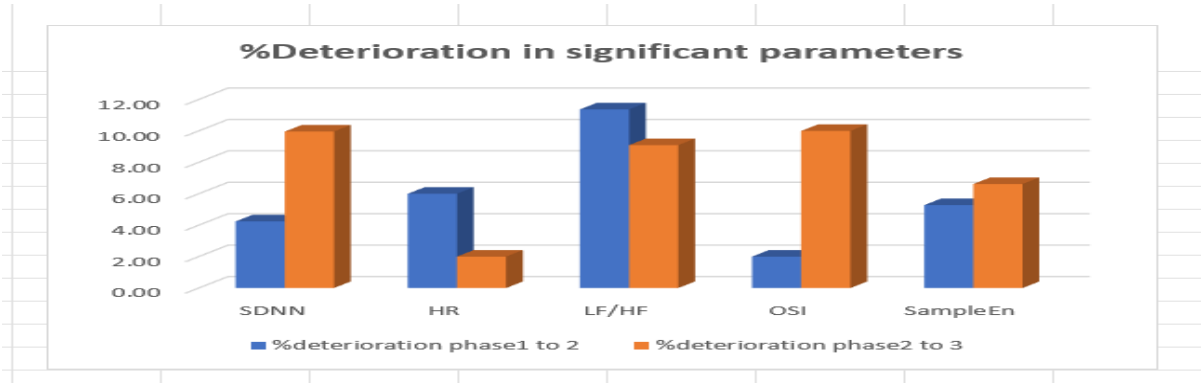

Figure 10: Percentage Deterioration in HRV parameters

5.5 Formulated a regression analysis model for predicting ejection fraction from HRV parameter

ECG and 2D echo are the two noninvasive techniques for diagnosing cardiac diseases. As electrocardiography provides the electrical activity of heart, 2D echocardiography (echo) provides mechanical functioning of the heart, 2D echo is ten times costlier than ECG. Predicting high accuracy parameters of 2D echo from ECG (HRV) is necessary. This objective aims at helping the rural people to assess cardiac health with a degree of correctness equivalent to 2D echocardiography (Echo) using electrocardiogram (ECG) signals. Echo diagnosis provides more accurate results than ECG.

Data Collection:

We have collected ECG and 2D-echo data (of same subject) of diabetics and cardiac diseased subjects from B & J super speciality hospital, Navi Mumbai. ECG data is collected from 12 electrode ECG aquisition machine, based on PC ECG software. A 2D Echocardiography images were obtained from ultrasound machine from GE healthcare in the same hospital. 2D echo imaging provides the majority of information about cardiac structure and function in routine clinical studies [37]. Figure 11 shows sample 2D echo image of ventricle with all its parameter values [38].

Methodology:

The correlation between HRV parameters and 2D echo parameter were found to find the best match for prediction of Echo parameter from HRV parameter. Next we have used regression method to derive the relationship for predicting echo parameter from HRV parameters. The above procedure is conducted on cardiac diseased and diabetic subjects.

LVEF calculation from 2D echo image: Figure 12 shows the LVEF calculation by Teicholz method. The 2D echo parameter, left ventricle ejection fraction is calculated from [39, 40]) as follows:

$$LVEF(\%) = (LVEDV - LVESV)/LVEDV * 100 \tag{2}$$

where, LVESV= left ventricle end-systolic volume and
LVEDS= left ventricle end diastolic volume.

ESV and ESV are calculated using the Teichholz correction [41].

$$EDV = 7/(24 + EDD)EDD^3 \tag{3}$$

and

$$ESV = 7/(24 + ESD)ESD^3 \tag{4}$$

where, EDD=end diastolic dimensions and ESD=end systolic dimensions.

Normal values of ejection fraction are approx.55%-65% [39] for healthy subject.

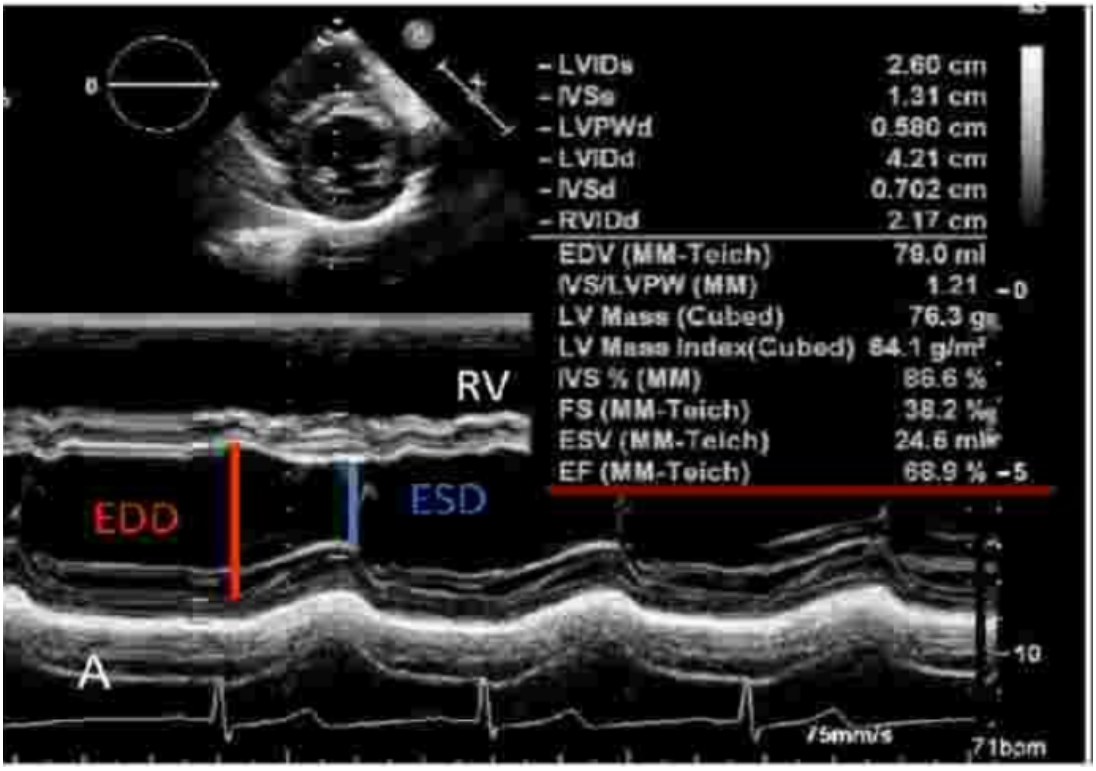

Figure 11: Echocardiographic evaluation of ventricular function

Correlation between LVEF and LF/HF Since the research aims to evaluate low-cost HRV parameters from expensive 2D-echo tests, a correlation between HRV and Echo needs to be evaluated. Correlation shows whether and how strongly a pair of variables are related. It is defined in [2] and formula is as follows:

$$r_{XY} = \frac{\sum (x - \hat{x})(y - \hat{y})}{\sum ((x - \hat{x})^2)((y_i - \hat{y})^2)} \tag{5}$$

Different combinations of ECG HRV and 2D Echo parameters were tried and correlation in each combination is noted. The maximum correlation was observed for LVEF and LF/HF combination. Pearson's correlation coefficient was performed to determine the correlation between LVEF and LF/HF.

Mathematical model for predicting LVEF from LF/HF: Because there is a strong correlation between LF/HF and LVEF, it is possible to develop a mathematical model for predicting LVEF (Echo) from LF/HF (ECG-HRV). To derive the relationship between these two variables, several regression models were tested to obtain the best fit model. Regression analysis explores the relationship between a quantitative response variable (here LVEF) and one or more explanatory variables (here LF/HF). The coefficients in the equation are estimated to minimize the sum of the squared error between the observed and expected values [42] of LVEF. The same procedure

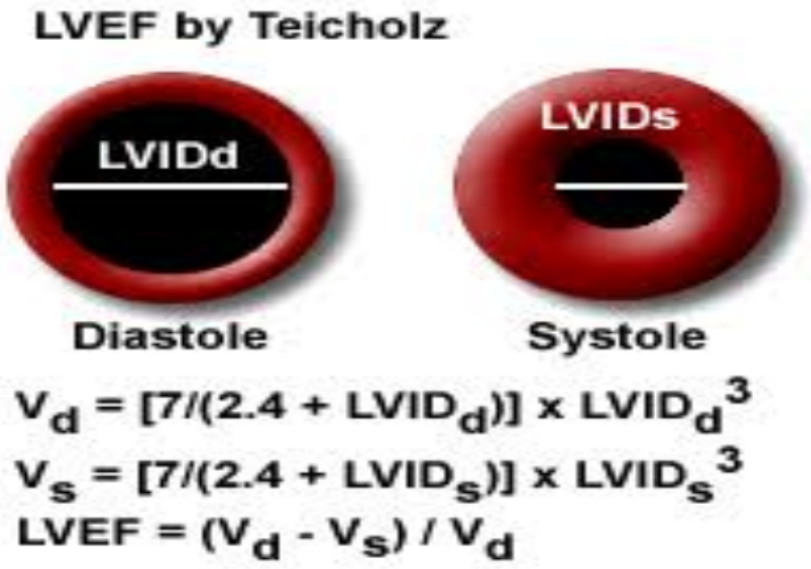

Figure 12: LVEF calculation by Teicholz method

Results:

Table 7 shows different models with their equation and R^2 value. The models are arranged in ascending order of their goodness of fit test, the R^2 value. Logarithmic and linear regression models are simple to implement but give smaller R^2 value (R^2 = 0.7914 and $R^2 = 0.9347$). The goodness of fit (R^2=0.9785) was found with polynomial regression with a degree of six, but is complex to implement therefore the final mathematical model is chosen as nonlinear regression model.

The correlation between ECG-HRV (LF/HF) and Echo (LVEF) is obtained as 74.4% and 83% in diabetics and cardiac diseased subjects. With this good correlation value we evaluated the mathematical model as shown in table7. The best fit model obtained is polynomial regression with degree four which provides maximum R squared value equal to 97.85%, but is more complex. The best fit model for cardiac diseased subjects is nonlinear regression as shown in figure 14 with 99.96% accuracy. So together we chose the best fit model as nonlinear regression.

Table 7: Mathematical models for prediction of LVEF with goodness of fit value

S.No.	**Regression Model**	**Equation**	R^2 **value**
1	Logarithmic regression	$y = 14.933ln(x) + 2.04170.7$	91.4
2	Linear regression	$y = 3.1896x + 5.6191$	0.9347
3	**Nonlinear regression**	$y = c_0 + c_1x - c_2 * exp(-c_3^x)$	**0.9454**
4	Polynomial regression with degree 6	$y = 0.0014x^6 - 0.057x^5 + 0.8897x^4 - 6.6652x^3 + 24.86x^2 - 40.371x + 33.317$	0.9785

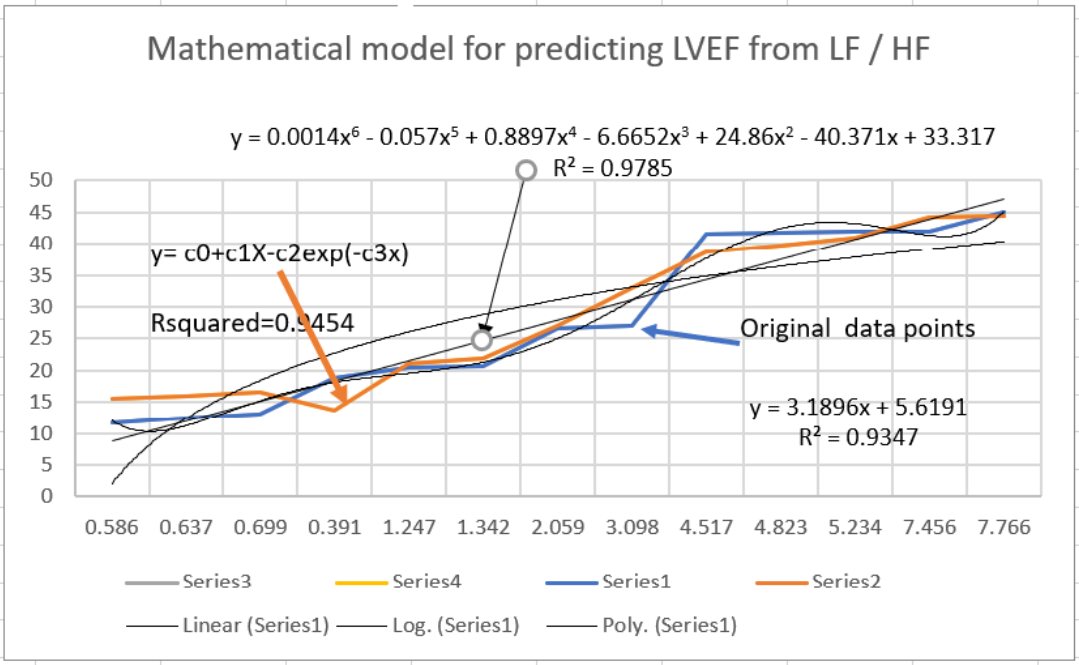

Figure 13: Regression model for diabetic subjects

Discussion

: The correlation between HRV parameter LH/HF and 2D echo parameter LVEF obtained is high. It is equal to 79% in case of diabetes and 83% in cardiac diseased. This implies prediction of one parameter from other. As the objective is to find the low cost HRV parameters from high cost 2D echo parameters we tried with logarithmic regression, linear regression, Non-linear regression and polynomial regression and calculated error value R^2 called coefficient of determination to find the best fit model. Greater the value of R^2 (maximum= 1), closer the predicted model to the original one [43]. In case of diabetic subjects the best fit model is obtained using polynomial regression with degree six with $R^2 = 97.85\%$. In case of cardiac diseased subject the best fit model is obtained from nonlinear regression with $R^2 = 99.99\%$. Combining the two results we conclude the best fit model for predicting HRV from 2D echo is obtained using nonlinear regression. The LF/HF ratio i.e. sympatho-vagal balance is proportional to LVEF, as high value in these parameters is sign of good cardiac health. This model can be used in rural areas where 2D echo facility is lacking or non-affordable. Therefore, it is helpful to economically weaker people for better cardiac disease diagnosis.

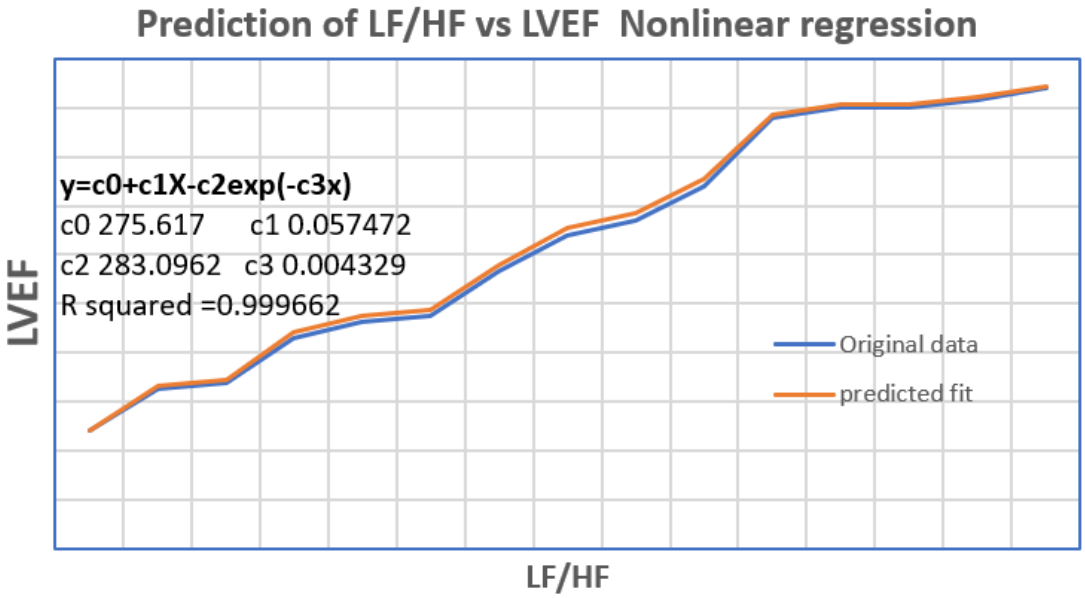

Figure 14: Nonlinear Regression model for Cardiac Diseased subjects

6 Conclusion

This thesis presents the analysis of cardiac health in cardiac diseased and diabetic subjects. We have carried out statistical analysis of HRV parameters for separation of cardiac and diabetic subjects. WE found that SDNN, NN50,HF,LF/HF,SD1, SD2, and ApEn are significant to separate these subjects. Further more we have also used used a machine learning technique for classifying these subjects. Our classification model has an accuracy of 93.58%.

Orthostatic stress index (OSI) ranks the subjects from high risk to low risk. Our experimental results showed that OSI is negative in cardiac diseased subjects, negative and positive in diabetics and positive in healthy or normal subjects.

Further LF/HF and OSI are most sensitive parameters and show deterioration or improvement in cardiac health. Further the nonlinear regression model developed predicts ejection function from LF/HF

7 Future scope

Number of classes can be increased based on different condition of patients, as diabetics with hypertensive, diabetics with cardiac diseases, diabetics, cardiac diseases. A detailed study of three point analysis over variable duration shall give more accurate prediction due to diabetes

8 Publication

1. U. Shirole, M. Joshi, and P. Bagul, "Cardiac, diabetic and normal subjects classification using decision tree and result confirmation through orthostatic stress index", *Informatics in Medicine Unlocked*, 17, 100252, 2019. (Impact factor= 2.11) **Scopus indexed**

2. U. Shirole, M. Joshi, and P. Bagul, "Linear and nonlinear analysis of cardiac and diabetic subjects," in *International Conference on Intelligent Information Technologies*, pp. 130–140, **Springer**, 2018.

3. U. Shirole, M. Joshi, K. Desai, and P. Bagul, "Cardiac autonomous function assessment in congestive heart failure using hrv analysis," *Int. J. Scientific Eng. Res*, vol. 8, no. 11, 2017. (Impact factor= 3.8)

4. U. Shirole and M. Joshi, "A mathematical model for prediction of LVEF from ECG in a three-point deterioration study of cardiac health in diabetics," **Scopus indexed** *International Journal of Advanced Research in Engineering and Technology*, vol. 11, no. 12,pp. 1846–1854, 2020. (Impact factor= 10.94)

5. U. Shirole and M. Joshi, "Time Domain Analysis of Heart Rate Variability: An Approach for Cardiac Stress Assessment" in *International Conference on Nascent Technologies in Engineering*, Navi Mumbai, **IEEE**, 2021.

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